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PATENT

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT:	Martinez, *et al.*	CONFIRMATION NO.:	2977
APPLICATION NO.:	10/751,736	GROUP NO.:	1642
FILING DATE:	January 6, 2004	EXAMINER:	Yao, Lei
TITLE:	Compositions and methods for diagnosing and treating colon cancers		

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF ROBERT VINCENT MARTINEZ UNDER 37 C.F.R. § 1.132

Sir:

I, Robert Vincent Martinez, hereby declare as follows:

1. I am a coinventor of the above-referenced patent application.

2. I hold a Ph.D. in genetics from Thomas Jefferson University. I studied gene expression as a Post-Doctoral Fellow at the Dana-Farber Cancer Institute, where I worked from 1997-2001, including the use of oligonucleotide microarrays to study the expression of genes responsive to a transcription factor. I continued to study gene expression patterns as a scientist at Wyeth Research, where I have worked since 2001 and am now a Principal Research Scientist. I author peer-reviewed articles and give presentations relating to gene expression patterns.

3. I have been asked whether, in view of my knowledge of the art, I would have expected, in January of 2004, a gene whose mRNA levels are elevated in colon cancer tissue compared to disease-free colon tissue would also have elevated amounts of the polypeptide encoded by that mRNA in colon cancer tissue.

4. In my experience, and given my knowledge of the art, I would have considered it more likely than not, in January 2004, that a gene that is transcriptionally upregulated in colon cancer tissue compared to disease-free colon tissue, thus having a greater amount of mRNA for that gene, would also have a greater amount of the polypeptide encoded by that mRNA. Although it is known that that protein levels can also be regulated at the level of translation of an mRNA or at the level of protein stability, within a given tissue or cell under two different conditions, one of which is associated with transcriptional upregulation of a gene, I would expect a greater amount of encoded protein to result from a greater amount of mRNA.

5. For example, inducible promoters were known and used, prior to January 2004, to drive higher polypeptide expression in the cells and tissues into which they were introduced. I successfully used one such system during my work at the Dana-Farber Cancer Institute, where I worked from 1997-2001. The expectation, when using an inducible promoter, was the use of such a promoter would result not only in an increase in mRNA transcription from the gene to which the promoter was linked but also in a corresponding increase in the level of the polypeptide encoded by that mRNA. Analogously, a scientist in 2004 would have expected that upregulation of mRNA transcription from a specific gene in colon tissue (*e.g.* in colon cancer) would result in a greater amount of the polypeptide encoded by that mRNA in the colon tissue.

6. All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true. These statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the present application or any patent issued in reliance thereon.

Date: January 9th 2007

Robert V. Martinez, Ph.D.